INFANTILE SCURVY

III. ITS INFLUENCE ON GROWTH (LENGTH AND WEIGHT)*

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In two previous papers[1] on this subject it was shown that pasteurized milk, that is, milk heated to 145 F. for thirty minutes, gradually induces infantile scurvy, unless antiscorbutic diet is given in addition. The fact that this disorder quickly yielded to the substitution of raw for pasteurized milk, or to the addition to the diet of an ounce of orange juice, or the juice of orange peel, was regarded as satisfactory evidence of the true scorbutic nature of the disturbance. The type of malnutrition which gradually develops from a diet of pasteurized milk may be termed subacute scurvy, as it takes some months to develop and, as a rule, does not manifest the pronounced symptoms characteristic of the classic case. In some instances, however, we encounter subperiosteal hemorrhages and the hemorrhagic gums typical of this disorder. That infantile scurvy is not met with more commonly, in view of the widespread use of pasteurized milk as a food for infants, may be ascribed to the fact that orange juice or other antiscorbutic food is so generally given in addition to milk. In other words, although pasteurized milk is to be recommended on account of the safety which it affords, it must be regarded as an incomplete food for infants. That the disease developing under these conditions is subacute in nature is to be attributed to the fact that the "vitamins," which are not overabundant in commercial milk, are not entirely destroyed by pasteurization, so that the infant receives day by day a small amount of these essential substances.

It will be remembered that these cases of scurvy arose in an institution where the use of orange juice was discontinued, in view of the report of the Commission on Milk Standards to the effect that milk does not suffer a destruction of enzymes or other chemical constituents in the course of pasteurization. In the first paper the nature of the hemorrhagic condition was studied, the question of involvement of the blood or of the blood vessels. In the subsequent paper the symptoms of infantile scurvy were shown to bear an intimate relationship to those

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1. Hess, A. F., and Fish, M.: Am. Jour. Dis. Child., December, 1914, viii, 386. Hess, A. F.: Jour. Am. Med. Assn., 1915, lxv, 1003.

of other deficiency diseases, more particularly beriberi. It was pointed out that scurvy should no longer be regarded clinically as a disorder characterized merely by hemorrhages, nor from a pathologic viewpoint merely as one manifesting changes in the bones, but that signs and symptoms of involvement of the heart (enlargement of the right ventricle and tachycardia) and of the peripheral nerves are also evident, so that a broader aspect is demanded. This paper, the third in the series, which is based mainly on the same cases which formed the groundwork of the previous studies, shows how these infants reacted in their growth to alterations in diet, how they grew on a diet consisting of pasteurized milk, sugar and cereal, when they were at the same time receiving orange juice, when the orange juice was discontinued, and when this juice or the juice of the orange peel was again added to the diet. These infants offered a particularly favorable opportunity for observations of this kind because they entered the institution at an early age and remained there for one or more years, and also because they were most carefully observed, weighed daily and measured on admission and every fortnight subsequently. It was thus possible to chart their growth for more than a year and to compare their progress with that of the other infants in the institution. As far as we are aware, no study of this kind has been attempted in connection with scurvy, although it has long been known that the development of the scorbutic condition is generally accompanied by a cessation of gain in weight. Particular interest would seem to be given this investigation as the subacute type of scurvy must be considered not only the most common form of the disorder, but that which passes most often unrecognized. The opportunity presented itself to probe farther into this question of growth and to determine whether there is not likewise a stunting of the normal increment of the skeleton, an interference with the increase in length. This part of the study was judged to be of greater biologic interest than a mere observation of the effect on weight, as it is well established that infants are particularly tenacious of their impulse to grow in length, and are not readily affected in this respect by nutritional disorders, even such as reach a considerable degree of intensity. As Birk[2] has shown, extreme undernourishment is necessary to bring about stunting. In animals, Aron[3] demonstrated that lack of nutrition led to a decrease of the fat and of the muscle in the body, but that under such conditions the skeleton continued to grow, and the ash content of the body to increase. If, therefore, this function of the body were affected, we must consider that the metabolism must be profoundly disturbed, and the deficiency of nutritional substances far reaching.

2. Birk, W.: Berl. klin. Wchnschr., 1911, No. 27.

3. Aron, H.: Biochemie des Wachstums des Menschen und der hoeheren Tiere, Gustav Fischer, 1913, p. 58.

First, as to growth measured by weight, the various charts (Figs. 1 to 4) accompanying this article show the effect in this regard. It will be noted that although the infants continued to gain for a month or two following the discontinuance of orange juice, a decided flattening of the weight curve gradually set in, an almost constant level being maintained for weeks and months. This stationary period persisted until antiscorbutic food was once more added to the diet, when a sudden rise made itself evident. This gradual cessation of gain and sharp reaction may be stated to have been the rule, as there was but one instance in which an infant continued to gain for months in spite of the lack of antiscorbutic food. It will be seen from these charts that there was no permanent retardation of weight; in other words, the growth impulse of the body remained unimpaired and had been merely in an inactive or quiescent state. When orange juice was given once more, the rate of growth was abnormally great. There was supergrowth. Furthermore, after a period of extended observation of six months or more, it has been found that this increased rate of growth is maintained until the infant reaches a weight normal for its age. These charts seem to require but little elucidation. We may add that orange juice and orange peel juice, an infusion of one ounce of orange peel in two ounces of water, were equally efficacious in bringing about a sharp increase in weight, and that these substances apparently did not lose their potency by being boiled.

Two cases should be mentioned especially, as they represent a clinical aspect somewhat different from the others. These infants were under 6 months of age and had never received orange juice. It was possible in these instances to observe for how long a period infants will continue to gain steadily in weight on pasteurized milk before it becomes necessary to add orange juice to their diet, and to judge whether they gradually manifest a lack of gain which can be obviated by giving an antiscorbutic foodstuff. It was found that at about the seventh or eighth month a gradual but definite falling off was evident, and that this deficiency was at once corrected by adding orange juice. Figure 3 represented this condition very clearly. We note here an infant who gained about one half pound during the months of February, March, April and May, but who in June, when given boiled orange peel juice or orange juice, gained two pounds within a month. There were no other scorbutic signs or symptoms and no loss of appetite during the months of February and March, although the baby was suffering from a progressive form of scurvy. It is probable that this case and a similar one which we encountered are not solitary instances of this kind of reaction, but that many infants fail to gain at this period, the third quarter of the first year of life, for the want of this essential substance in their food, and that unconsciously this deficiency is reme-

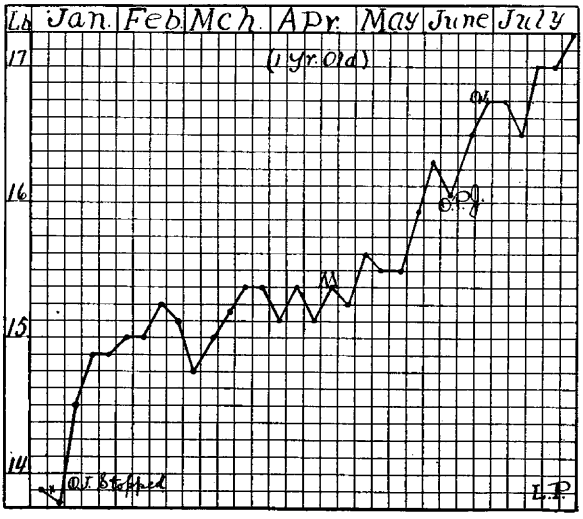

Fig. 1.—Marked gain in weight on orange peel juice and orange juice after lack of gain for three months.

In this and the following figures *O. J.* indicates orange juice; *M.* wheat middlings, and *O. P. J.* orange peel juice.

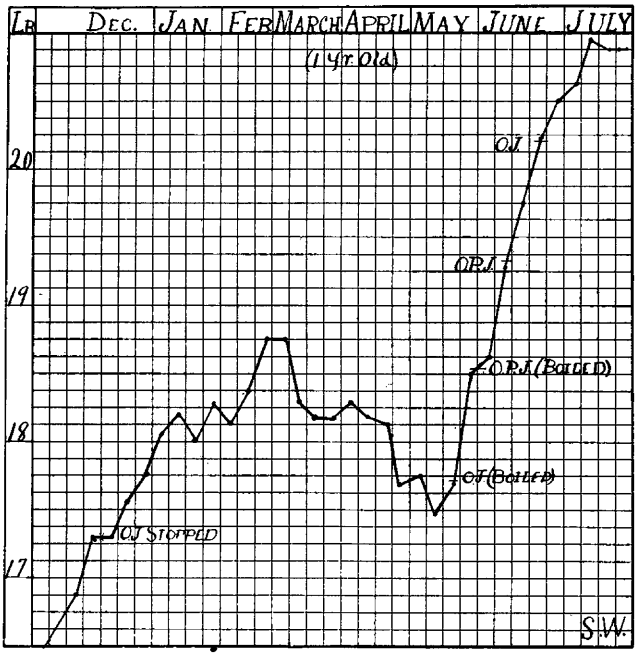

Fig. 2.—Loss of weight checked by boiled orange juice and boiled juice of orange peel.

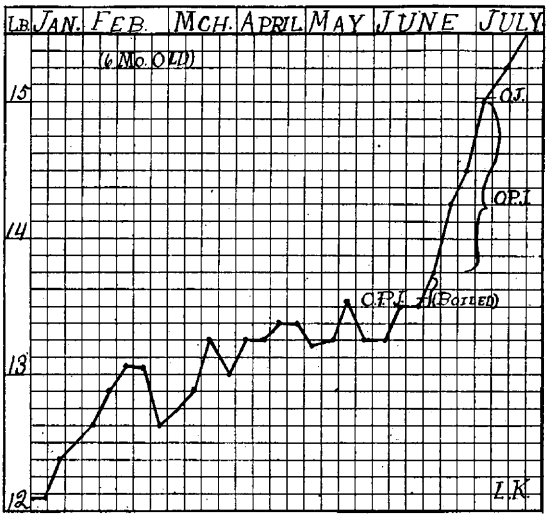

Fig. 3.—Latent scurvy in young infant who had never received orange juice. Scorbutic nature of growth disorder proved by sharp rise in weight on addition of antiscorbutic food to the dietary of pasteurized milk.

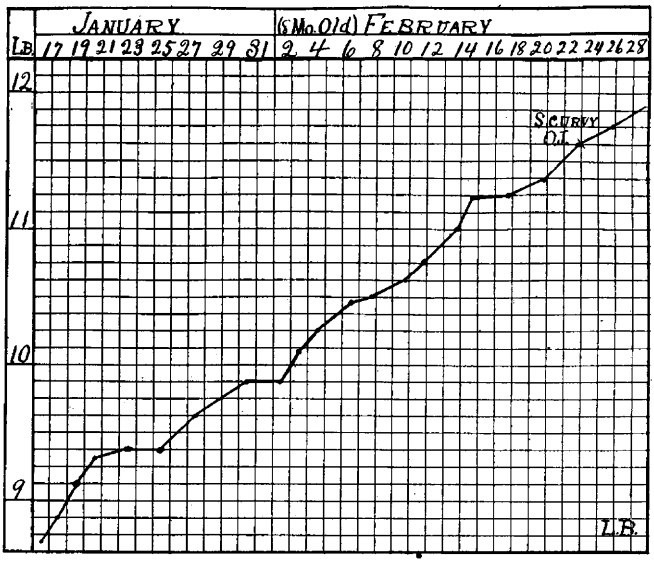

Fig. 4.—Development of scurvy in spite of normal gain in weight in a baby who had been underfed since birth.

died by adding vegetables and fruit to their dietary. We would therefore urge that antiscorbutics, for instance orange juice, be given infants at an early age. At present, the rule may be said to be to add fruit juices to the dietary at about the sixth month. This period has been chosen as the proper one, probably because scurvy rarely develops during the first half year of life. However, when we reflect that this time incidence is due to the fact that the infant is protected for the first few months of life by the supply of antiscorbutic material which it has received from the mother, and that there must be a constant negative balance of these essential substances dating from the earliest beginning of artificial feeding, it would seem as if a corrective dietary, that is to say, an antiscorbutic food, should be given as soon as practicable. There is no reason that I know of why an infant should not receive orange juice when it is a month old, and, as we have seen, there are strong arguments in favor of such a procedure.

It may be enunciated as a rule, embracing a few exceptions, that the development of the scorbutic state is generally accompanied by a failure to gain in weight. Under certain conditions, however, the weight may follow a perfectly normal course during the entire period. This observation has, from time to time, been made by others, but has received no particular consideration. It may be well therefore to cite in some detail a case of this kind, and discuss one cause of this apparently paradoxical course of events. Figure 4 illustrates this clinical paradox. The baby to whom it refers was admitted to the institution in January and was stated to be only four months of age. As a matter of fact, as we learned later, he was seven and a half months old. Toward the end of February, when he had been in the institution two months, and in spite of constant and normal gain in weight, to our surprise he manifested unmistakable signs of scurvy—peridental hemorrhage over the upper incisor teeth, which were erupting, and tenderness of the lower ends of the femora. The scorbutic nature of these signs were substantiated by their prompt subsidence on the administration of orange juice.

How is this phenomenon to be explained, normal growth during the development of scurvy, one of the classical nutritional disorders of infancy? The solution is to be found in a careful consideration of the previous diet of the baby. On investigation we found that it was born on June 5, 1915, at term, weighing six pounds, but was never nursed. For the first two weeks it received an indefinite formula prepared by the mother. From June 21 to August 19, that is, for a period of about two months, it was given a formula composed of one-fourth milk, three-fourths water, and 1.5 per cent. sugar, two ounces every three hours. In other words, it was greatly underfed for these two months. In August it weighed 8 pounds, 5 ounces. From August 19 to 27 the

formula was 30 ounces water, 12 ounces milk, and about 1 per cent sugar, four ounces being fed every three hours. This resulted in loss of weight, the baby weighing 7 pounds 15 ounces. On September 7 the formula was made one-half milk, one-half water and 1 per cent. sugar, four ounces every three hours. The underfeeding continued. On December 5 it was transferred to a hospital, where it was given a malt soup preparation for one month. It developed gastro-enteritis on January 17. As the chart shows, the child was admitted to the Hebrew Infant Asylum, weighing about 8¾ pounds at the age of 7½ months.

If we consider the feeding of this infant, we realize that it had been almost continuously undernourished, receiving an insufficient amount of fats and carbohydrates at almost all times. At the asylum the baby was put on Schloss milk, a food containing about 4 per cent. fat and about 6 or 7 per cent. carbohydrates, seven feedings of 4 ounces in the twenty-four hours. On this it remained and, as will be seen, made steady gains until it developed scurvy toward the end of February.

This baby must be regarded as having been partially starved throughout the period following birth, with the result that on receiving a diet rich in fats and carbohydrates, foodstuffs which bring about a marked increase in weight, the reaction of the tissues was necessarily prompt and prolonged. It explains this type of case, showing that if an infant has received insufficient food, we can compel growth simply by increasing the caloric value of the dietary, notwithstanding the fact that scurvy is developing day by day. It also brings out the salient fact that more than a single cause exists leading to a repression of growth, and that therefore lack of growth must be differentiated if it is to form the basis of study. A deficiency of scurvy vitamins is one cause, lack of sufficient or adequate food is another, and, no doubt, there are still other inciting factors. Whether or not growth occurs, and to what extent, depends on the resultant stimulation which can be brought about by these various impulses. In this instance the primary growth impulse which follows a diet containing a sufficient number of calories had been held in abeyance for so many months through starvation, that when it was once more stimulated to full activity by a liberal diet, it was able to overcome the growth repression which ordinarily accompanies the development of the scorbutic condition.[4]

The foregoing illustration must make it clear that growth does not play an essential or elemental part in the constitution of infantile

4. This phenomenon probably also holds good for scurvy in the adult. A scorbutic condition may result from a lack of fresh food; but if the person has been markedly underfed, there may be a gain in weight coincident with the development of the scorbutic condition, provided liberal diet is given, including plenty of carbohydrate and fat.

scurvy. It must likewise render it evident that this study cannot be regarded as concerned with growth in general, but only with the effect of infantile scurvy on growth, as various disorders may affect this function. That such is the case is well known to clinicians and has been shown admirably in relation to animals in the recent investigations of Osborne and Mendel, of McCollum and others, which showed that growth was retarded or stimulated at will by means of diet. The results of these workers cannot, however, be considered as having any bearing on scurvy, for scurvy and growth stunting are by no means identical, either in animals or in infants. It would seem that these remarks are timely in view of a recently published study by McCollum and Davis,[5] in which they show that the growth factor in milk is closely linked to its casein content, and preface their report by drawing an analogy to infantile scurvy, although apparently none of the animals showed any signs of a scorbutic condition.

Looking at this question from the reverse point of view, one sees clearly that factors which stimulate growth are not necessarily antiscorbutic. For example, McCollum and Davis[6] showed that butter fat, even after it had been heated to a high degree, was able to induce growth, and Osborne and Mendel[7] showed that this fat can be subjected to steam and not lose its growth producing power. It is nevertheless evident that butter fat in pasteurized milk does not possess sufficient antiscorbutic properties to prevent the development of scurvy, and that substances such as lysin and tryptophan, which possess marked growth promoting power, and which were present in considerable amount in our diet, were unable to make up for the dietary deficiency and bring about growth. Furthermore, cod liver oil has been found to possess growth-promoting qualities of a high degree, but there is no question that this substance, as has been shown elsewhere,[1] is incapable of preventing the development or accomplish the cure of scurvy. Before reporting additional observations as to the influence of scurvy on growth, let me add that all of the infants under consideration obtained plenty of milk, and all the older ones received cereal in addition. Particular attention was given to their obtaining a sufficient quantity, so that the factor of an insufficient diet might not enter into the question. To this end, when orange juice was discontinued, more cereal was given or the strength of the milk mixture was increased in many instances. In those cases in which there was loss of appetite, particular effort was made to have the infants take the full quantity of food, and, although the total amount consumed in many cases was not quite as much as when they were well, it nevertheless equaled that

5. McCollum, E. V., and Davis, M.: Jour. Biol. Chem., November, 1915, p. 247.
6. McCollum, E. V., and Davis, M.: Jour. Biol. Chem., 1913, xv, 167.
7. Osborne, T. B., and Mendel, L. F.: Jour. Biol. Chem., May, 1915, p. 381.

which many infants in the institution consume and on which they continue to grow.

There is no doubt that considerable of the supergrowth which so clearly follows the giving of orange juice or its equivalent is due to an increased consumption of food. However, it would be a mistake to consider that such is entirely the case. We have reproduced two charts to illustrate this point. The first (Fig. 5) is a daily weight chart of an infant with mild scurvy, and shows the period preceding as well as

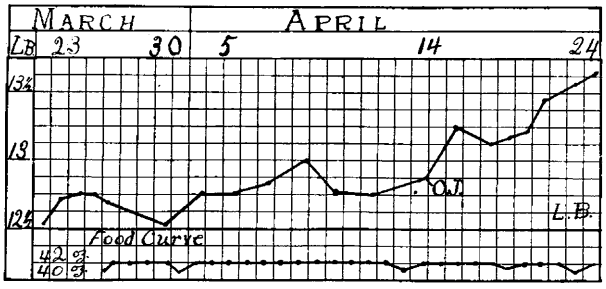

Fig. 5.—Same case as preceding. Detailed chart showing marked gain following the addition of an antiscorbutic to the diet, although amount of food remained the same.

Gain of 5 ounces in three weeks before, and 12 ounces in ten days after orange juice was given.

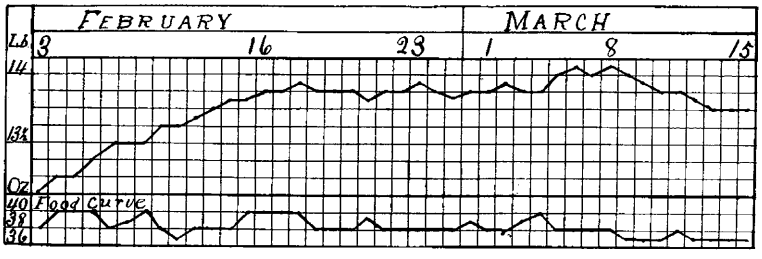

Fig. 6.—Section of a weight chart showing daily weighings during the period when gain still continued and when stationary plane was reached.

Note that the same amount of food was taken daily during the first two weeks of February, when the infant gained 12 ounces, as from the middle of February to the middle of March, when there was no gain whatever.

This baby had latent scurvy and responded promptly to orange juice.

that following the giving of orange juice, together with the food intake (Schloss milk). Although it will be seen that there was no change in the amount of milk taken before and after giving orange juice, there was a marked difference in the gain; the infant increased only 5 ounces in weight during the three weeks in which it did not obtain orange juice, and 12 ounces in ten days following its addition to the diet.

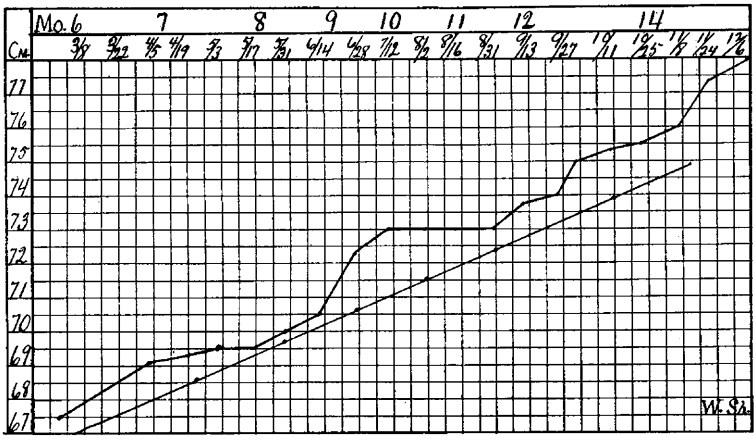

Fig. 7.—Growth in length from the sixth to the fifteenth month of healthy baby receiving orange juice. The lower line represents the average growth.

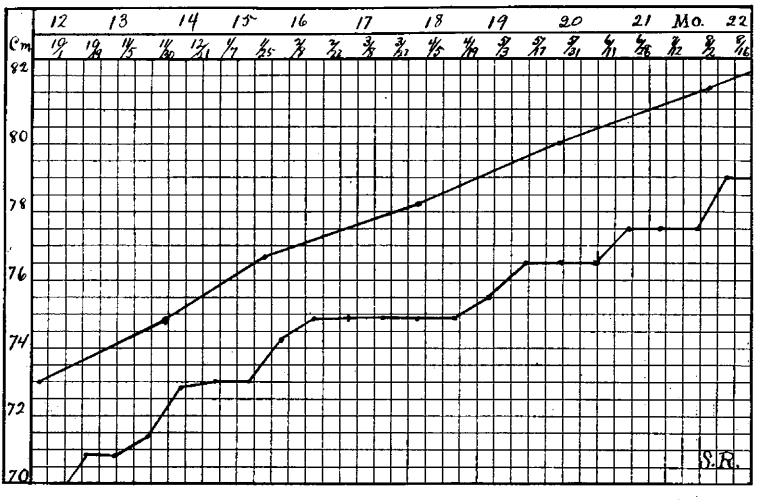

Fig. 8.—Growth in length from the twelfth to the twenty-second month of a very small, healthy baby receiving orange juice.

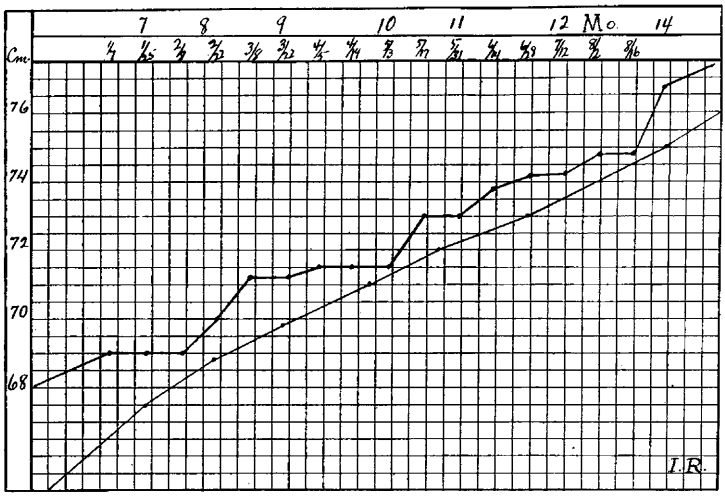

Fig. 9.—Growth in length from the seventh to the fourteenth month of a large healthy baby receiving orange juice.

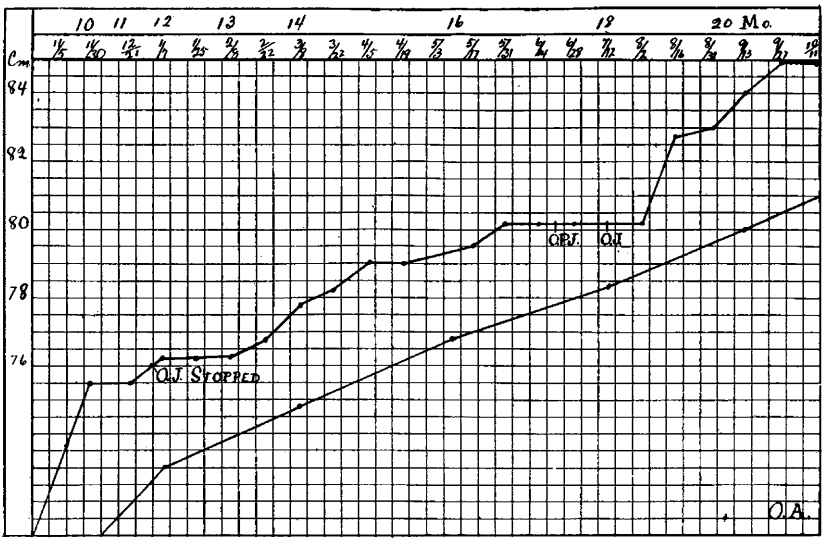

Fig. 10.—Growth in length for a period of five months during which no orange juice was given, compared with subsequent months when it was again added to the diet.

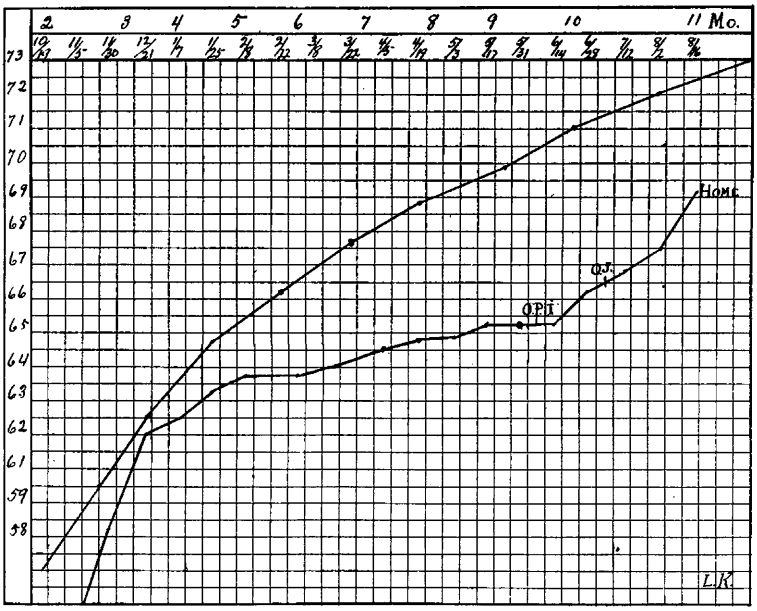

Fig. 11.—Length chart of young infant (illustrated in Fig. 3) who had never received orange juice. Marked reaction in growth in length when an anti-scorbutic was added to the diet.

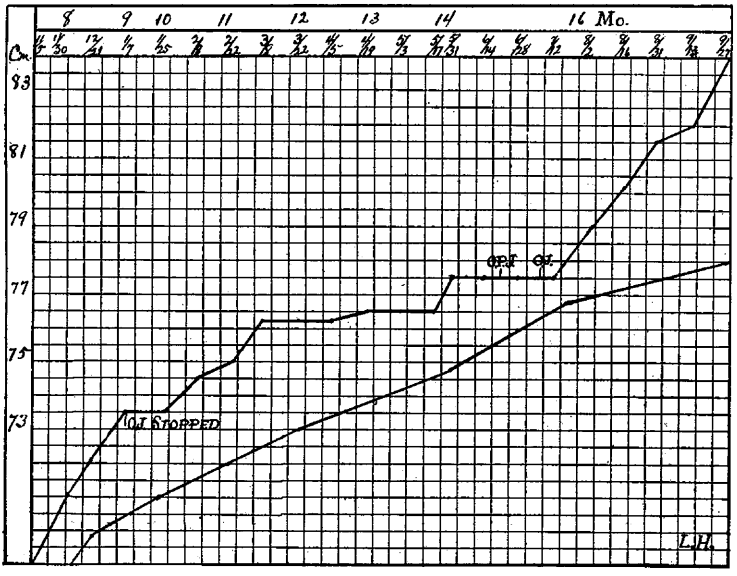

Fig. 12.—Showing retardation of growth in length during the period when no orange juice was given, and supergrowth when it was given once more.

Figure 6 shows another aspect of this question. It demonstrates that the period of gradual growth stagnation, on which infants fed entirely on pasteurized milk enter as the result of not receiving an antiscorbutic, is not due to a lack of food. Here we note the gradual inception of this stationary phase, from a period of gain, in spite of the fact that the intake of food remained undiminished. It is evident, therefore, that neither the lack of gain in the course of the development of infantile scurvy, nor the increase of weight coincident with its cure, can be considered to be dependent on the caloric value of the dietary.

As has been mentioned above, a study of the growth in length was also carried out, the measurements being taken fortnightly for over a year. In order to furnish a basis for comparison, the growth of ten normal infants who received orange juice, but otherwise the same diet, was followed at the same time. The charts which we reproduce clearly bring out the distinction between the two groups of cases. Figures 7, 8 and 9 illustrate the growth of the normal infants, and constitute a standard by which to judge the others. They portray a consistent, alhough slightly irregular, growth month by month. Quite in contrast to these curves are those depicted in Figures 10, 11 and 12, representing three infants who did not receive orange juice from January to May.

Figure 11, which represents growth in length complements Figure 3, representing growth in weight, and illustrates the case of a young baby who had never received orange juice, and developed a latent or rudimentary form of scurvy when about eight months of age. These three cases, when contrasted with the normals, leave no question that the scorbutic condition has a decided effect on growth in length as well as in weight, and that this impulse remains unimpaired in both respects and capable of quick response when the essential foodstuff is furnished.

CONCLUSIONS

Although pasteurized milk is to be recommended on account of the security which it affords against infection, we should realize that it is an incomplete food. Unless an antiscorbutic, such as orange juice, the juice of orange peel, or potato water is added, infants will develop scurvy on this diet. This form of scurvy takes some months to develop and may be termed subacute. It must be considered not only the most common form of this disorder, but the one which passes most often unrecognized. In order to guard against it, infants fed exclusively on a diet of pasteurized milk should be given antiscorbutics far earlier than is at present the custom, even as early as at the end of the first month of life.

In the course of the development of infantile scurvy, growth, both in weight and in length, is markedly affected. Under these conditions,

weight ceases to increase, and a stationary plane is maintained for weeks or for months. There is a quick response, however, on the administration of orange juice or its equivalent, indeed supergrowth is thereupon frequently manifested. If, however, an infant has been underfed, an increase in weight may continue throughout the development of the scorbutic condition. Cessation of growth, as well as marked increase in growth, may manifest themselves, although the caloric value of the food remains unchanged, depending merely on the withholding or the addition of essential foodstuffs to the diet.

Measurements showed that growth in length is also retarded during the protracted development of infantile scurvy. This is of greater biologic interest, as simple malnutrition usually does not affect this function in the infant. In this particular, supergrowth also follows the addition of the essential foodstuff, showing that the growth impulse has remained uninjured and has been merely held in abeyance.

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